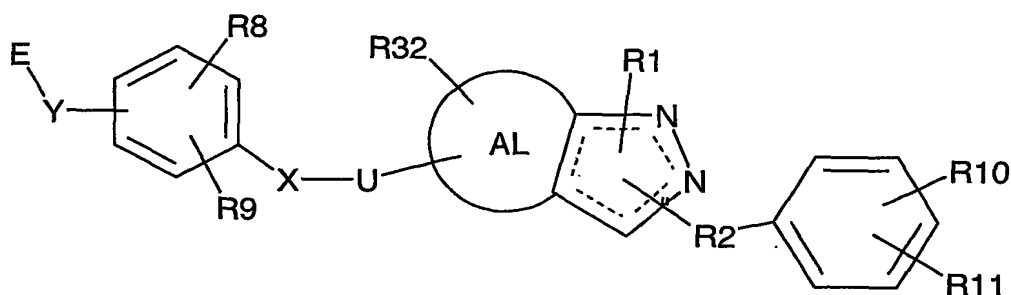


- 162 -

CLAIMS

What is claimed is:

1. A compound of the structural Formula I:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀₋₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉, NR₂₀SO₂R₂₁, SR₂₂, S(O)R₂₃, S(O)₂R₂₄, and S(O)₂N(R₂₅)₂; R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄ and R₂₅ are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

(c) R₂ is selected from the group consisting of C₀-C₈ alkyl and C₁₋₄-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;

- 163 -

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;

(f) Y is selected from the group consisting of C, NH, and a single bond;

5 (g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;

10 (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and

15 (iv) R4 is selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

20 (h) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;

(i) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, SR29, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C₁-C₄ alkylenyl, and C₁-C₄ alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

25
30

- 164 -

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R₁₃', COOR₁₄', OC(O)R₁₅', OS(O)₂R₁₆', N(R₁₇')₂, NR₁₈'C(O)R₁₉', NR₂₀'SO₂R₂₁', SR₂₂', S(O)R₂₃', S(O)₂R₂₄', and S(O)₂N(R₂₅')₂; and wherein aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R₂₈;

(k) R₁₂', R₁₂'', R₁₃', R₁₄', R₁₅', R₁₆', R₁₇', R₁₈', R₁₉', R₂₀', R₂₁', R₂₂', R₂₃', R₂₄', and R₂₅' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

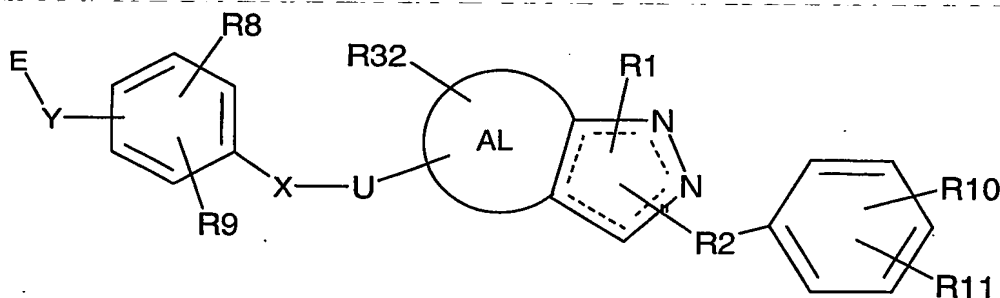
(l) R₃₀ is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents each independently selected from R₃₁;

(m) R₃₂ is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxy;

(n) AL is selected from the group consisting of a fused C₃-C₈ carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(o) ---- is each optionally a bond to form a double bond at the indicated position.

2. A compound of the structural Formula II:



- 165 -

and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R₁ is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R₁';

(b) R₁', R₂₆, R₂₇, R₂₈ and R₃₁ are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀₋₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉, NR₂₀SO₂R₂₁, SR₂₂, S(O)R₂₃, S(O)₂R₂₄, and S(O)₂N(R₂₅)₂; R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄ and R₂₅ are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

(c) R₂ is selected from the group consisting of C₀-C₈ alkyl and C₁₋₄-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R₃₀;

(f) Y is selected from the group consisting of C, O, S, NH and a single bond;

(g) E is C(R₃)(R₄)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;

(ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;

- 166 -

(iii) R3 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and

(iv) R4 is selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

(h) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;

(i) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, SR29, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C₁-C₄ alkylenyl, and C₁-C₄ alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

- 167 -

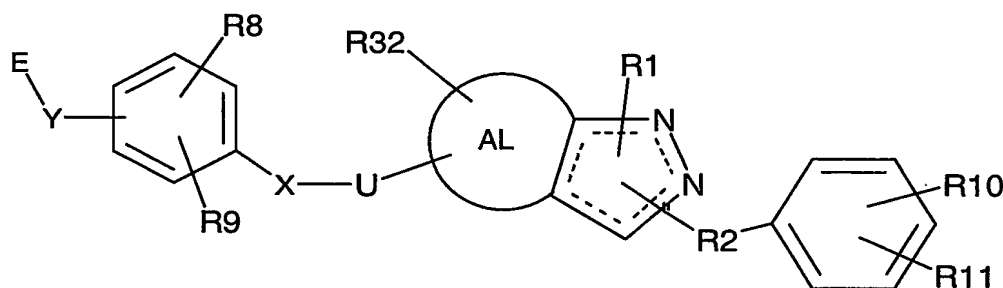
(l) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(m) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxy;

(n) AL is selected from the group consisting of a fused C₃-C₈ carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(o) ---- is each optionally a bond to form a double bond at the indicated position.

3. A compound of the structural Formula III:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀₋₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15,

- 168 -

OS(O)₂R16, N(R17)₂, NR18C(O)R19, NR20SO₂R21, SR22, S(O)R23, S(O)₂R24, and S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

- 5 (c) R2 is selected from the group consisting of C₀-C₈ alkyl and C₁₋₄-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;
- 10 (f) Y is selected from the group consisting of C, O, S, NH and a single bond;
- (g) E is C(R3)(R4)A or A and wherein
- (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally
- 15 substituted with from one to two groups independently selected from R⁷;
- (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;
- (iii) R3 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and
- 20 (iv) R4 is selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally
- 25 substituted with one to three substituents each independently selected from R26;
- with the proviso that when Y is O then R4 is selected from the group consisting of C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form
- 30 a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-

- 169 -

alkyl are each optionally substituted with one to three each independently selected from R26;

(h) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;

5 (i) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, SR29, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C₁-C₄ alkylenyl, and C₁-C₄ alkyl; R8 and R9 optionally combine to form a five membered
10 fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12'', C₀-C₆
15 alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-
20 alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

25 (l) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl- C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

- 170 -

(m) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxo;

(n) AL is selected from the group consisting of a fused C₃-C₈ carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

5 (o) ---- is each optionally a bond to form a double bond at the indicated position.

4. A compound as claimed by Claim 1 wherein X is -O-.

5. A compound as claimed by Claim 1 wherein X is -S-.

10

6. A compound as claimed by any one of Claims 1 through 5 wherein Y is O.

7. A compound as claimed by any one of Claims 1 through 5 wherein Y is C.

15 8. A compound as claimed by any one of Claims 1 through 5 wherein
wherein Y is S.

9. A compound as claimed by any one of Claims 1 through 8 wherein AL is a
fused phenyl.

20

10. A compound as claimed by any one of Claims 1 through 8 wherein AL is a
fused cycloalkyl.

11. A compound as claimed by any one of Claims 1 through 8 wherein AL is a
25 fused pyrimidinyl.

12. A compound as claimed by any one of Claims 1 through 8 wherein AL is a
fused pyridinyl.

30 13. A compound as claimed by any one of Claims 1 through 8 or Claim 15
wherein ---- is a bond to form a double bond at the designated location on Formula I.

- 171 -

14. A compound as claimed by any one of Claims 1 through 13 wherein E is C(R3)(R4)A.

5 15. A compound as claimed by any one of Claims 1 through 13 wherein E is A.

16. A compound as claimed by any one of Claims 1 through 14 wherein A is COOH.

10 17. A compound as claimed by any one of Claims 1 through 16 wherein R10 is haloalkyl.

18. A compound as claimed by any one of Claims 1 through 17 wherein R10 is CF₃.

15 19. A compound as claimed by any one of Claims 1 through 16 wherein R10 is haloalkyloxy.

20 20. A compound as claimed by any one of Claims 1 through 16 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR¹², C₁-C₆ alkoxy, C₁-C₆ haloalkyl, and C₁-C₆ haloalkyloxy.

25 21. A compound as claimed by any one of Claims 1 through 16 wherein R10 is selected from the group consisting of C₃-C₇ cycloalkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and aryloxy.

22. A compound as claimed by any one of Claims 1 through 21 wherein R8 is selected from the group consisting of C₁-C₃ alkyl and C₁-C₄ alkylenyl.

- 172 -

23. A compound as claimed by any one of Claims 1 through 21, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C₁-C₃ alkyl.

5 24. A compound as claimed by any one of Claims 1 through 22 wherein R29 is C₁-C₄ alkylenyl.

25. A compound as claimed by any one of Claims 1 through 22 and 24 wherein R8 is C₁-C₄ alkylenyl.

10 26. A compound as claimed by any one of Claims 1 through 22, 24, and 25 wherein R9 is OR29.

15 27. A compound as claimed by any one of Claims 1 through 22, 24, and 25 wherein R9 is SR29.

28. A compound as claimed by any one of Claims 1 through 22, 24 through 25 wherein R8 and R9 combine to form a fused bicyclic.

20 29. A compound as claimed by any one of Claims 1 through 28 wherein R1, R2, R3, and R4 are each independently selected from the group consisting of C₁-C₂ alkyl.

25 30. A compound as claimed by any one of Claims 1 through 28 wherein R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C₁-C₂ alkyl.

31. A compound as claimed by any one of Claims 1 through 28 and 30 wherein R2 is a bond.

30 32. A compound as claimed by any one of Claims 1 through 31 wherein U is C₁-C₃ alkyl.

- 173 -

33. A compound as claimed by Claim 32 wherein U is saturated.

34. A compound as claimed by any one of Claims 32 or 33 wherein U is substituted with C₁-C₃ alkyl.

5

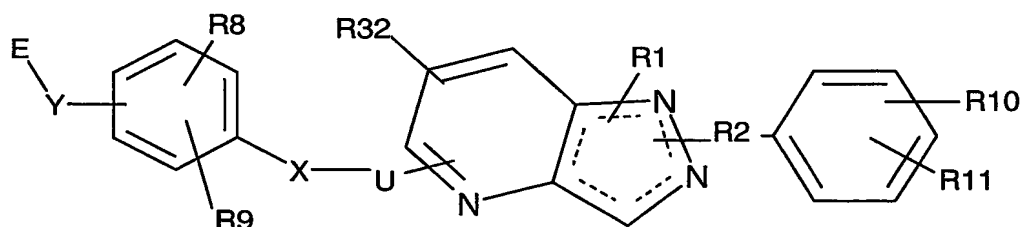
35. A compound as claimed by any one of Claims 1 through 34 wherein aliphatic linker is substituted with from one to four substituents each independently selected from the group consisting of R₃₀.

10

36. A compound as claimed by any one of Claims 1 through 33, 34, and 35 wherein one carbon of the aliphatic linker is replaced with an -O-.

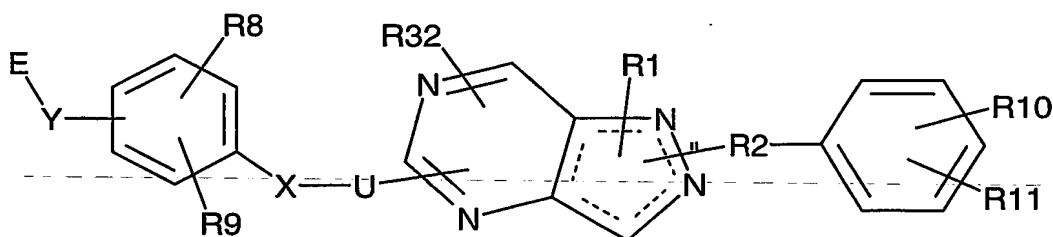
37. A compound as claimed by any one of Claims 1 through 4, 7, 8, 9, Claims 13 through 27, Claims 29 through 36 of the Structural Formula:

15



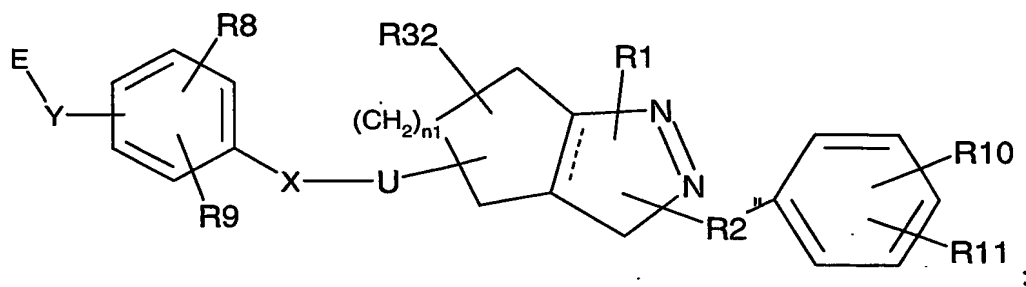
38. A compound as claimed by any one of Claims 1 through 5, 8, 9, Claims 12 through 27 Claims 29 through 36 of the Structural Formula:

20



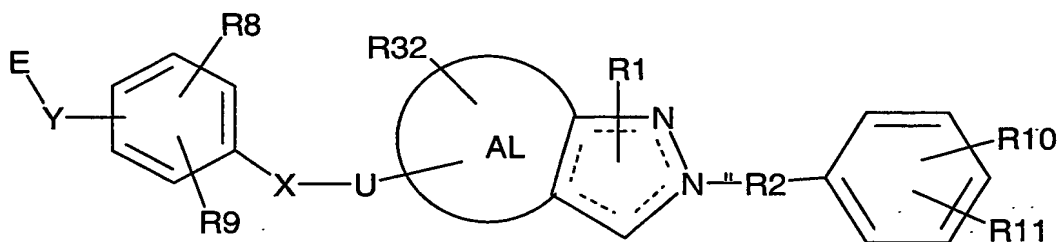
39. A compound as claimed by any one of Claims 1 through 11, 15, Claims 18 through 32, Claims 34 through 36 of the Structural Formula IV:

- 174 -

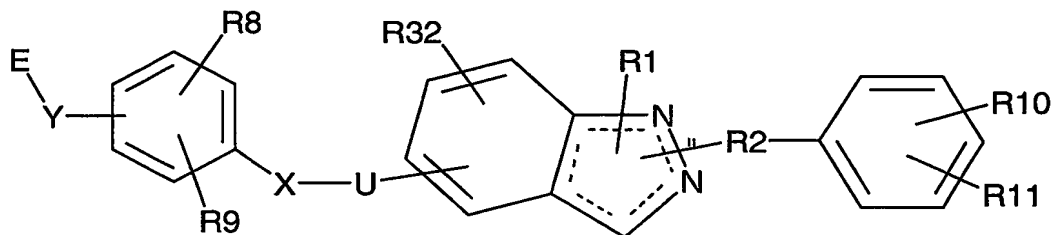


wherein n_1 is 1 to 5.

40. A compound as claimed by any one of Claims 1 through 13, 17 through 31, Claims 33 through 36 of the Structural Formula:



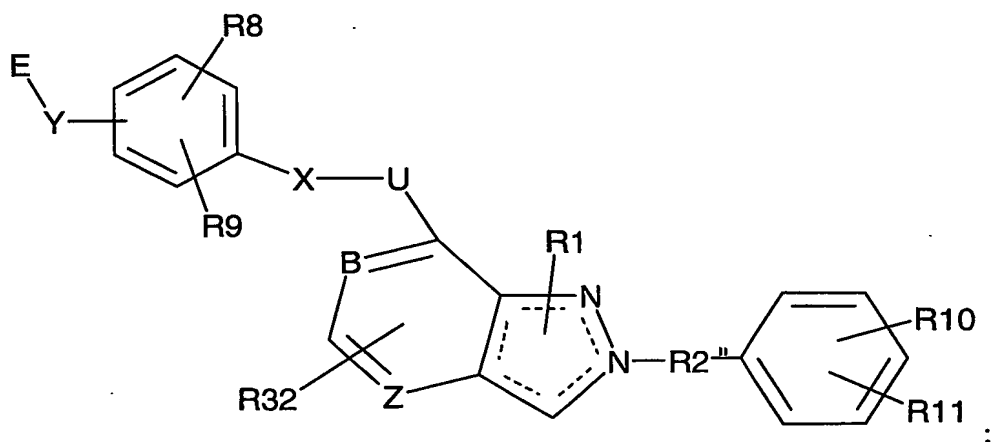
41. A compound as claimed by any one of Claims 1 through 13, Claims 17 through 31, Claims 33 through 36 of the Structural Formula:



10

42. A compound as claimed by any one of Claims 1 through 11, Claims 14 through 28, Claims 30 through 36 of the Structural Formula:

- 175 -

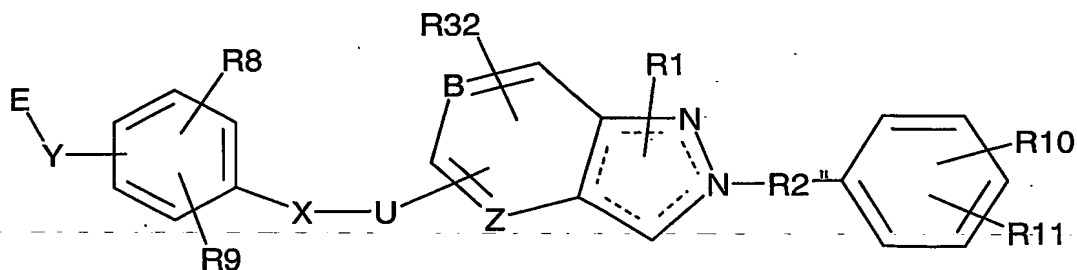


wherein B is N or C; Z is N or C, with the proviso that when Z is C then B is C.

43. A compound as claimed by any one of Claims 1 through 9, Claims 13 through 27, Claims 29 through 42 wherein X is S, Y is selected from the group consisting of C and O, E is CH₂COOH, and R2 is a bond.

44. A compound as claimed by any one of Claims 1 through 43 wherein R32 is hydrogen, R8 is hydrogen and R9 is C₁-C₄ alkyl.

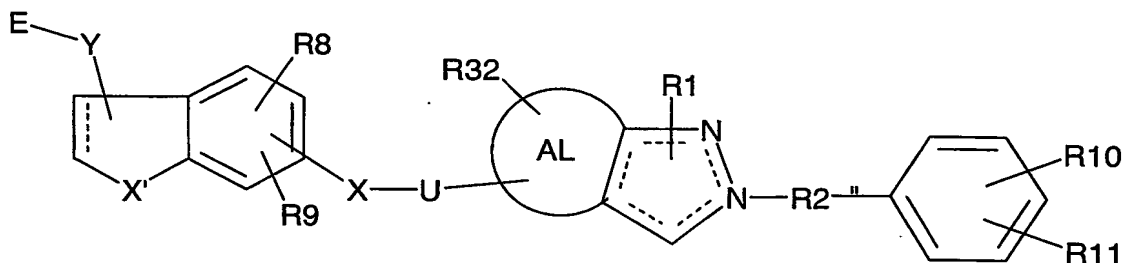
45. A compound as claimed by any one of Claims 1 through 13, 17, Claims 18 through 32, Claims 34 through 41 of the Structural Formula:



wherein B is N or C; Z is N or C, with the proviso that when Z is C then B is C.

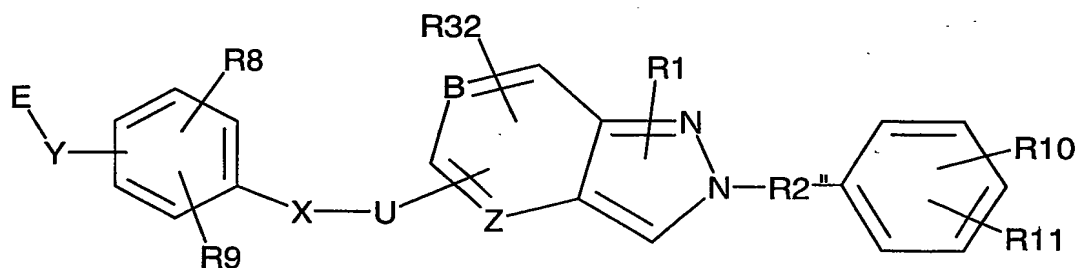
46. A compound as claimed by any one of Claims 1 through 28, Claims 30 through 37 of the Structural Formula:

- 176 -



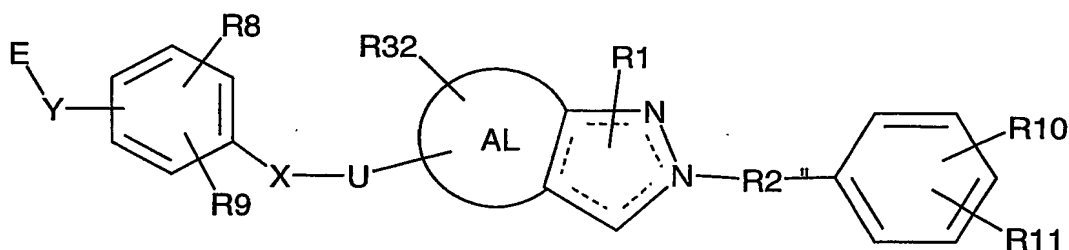
wherein X' is selected from the group consisting of O and S.

47. A compound as claimed by any one of Claims 1 through 13, 16, Claims 18 through 32, Claims 34 through 41 of the Structural Formula X:



wherein B is N or C; Z is N or C, with the proviso that when Z is C then B is C.

48. A compound as claimed by any one of Claims 1 through 13, 16, Claims 18 through 32, Claims 34 through 41 of the Structural Formula: XI:



49. A compound as claimed by any one of Claims 1 through 3 wherein the compound is selected from the group consisting of

2-Methyl-4-[2-(4-trifluoromethylphenyl)-2H-indazol-7-ylmethylsulfanyl]phenoxyacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2H-indazol-7-ylmethylsulfanyl]phenyl}propionic Acid;

- 177 -

2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenoxyacetic Acid;

5 3-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenylacetic Acid;

6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]benzo[*b*]thiophen-3-ylacetic Acid;

10 3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenyl}propionic Acid;

3-{2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenyl}propionic Acid;

15 (+/-)-2-Methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

20 (+/-)-2-Methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

(+/-)-3-(2-Methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenyl)propionic Acid;

25 (+/-)-2-Ethyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

(+/-)-6-{1-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-7yl]ethylsulfanyl}benzo[*b*]thiophen-3-ylacetic Acid;

30 (+/-)-3-(2-Methyl-4{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7yl]ethoxy}phenyl)propionic Acid;

35 (+/-)-3-(2-Ethyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxyphenyl)propionic Acid;

- 178 -

2-Methyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

5 2-Methyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

3-(2-Methyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenyl)propionic Acid;

10 2-Ethyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

15 6-{1-Methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}benzo[*b*]thiophen-3-ylacetic Acid;

2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxyacetic Acid;

20 3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenyl}propionic Acid;

2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxyacetic Acid;

25 3-{2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenyl}propionic Acid;

30 6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]benzo[*b*]thiophen-3-ylacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenyl}propionic Acid;

35 {6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]benzo[*b*]thiophen-3-yl}acetic Acid;

- 179 -

2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic
Acid;

5 2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic
Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-
ylmethylsulfanyl]phenyl}propionic Acid;

10 6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]benzo[*b*]thiophen-3-
ylacetic Acid;

15 2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic
Acid;

2-Ethyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic
Acid;

20 3-{2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-
ylmethylsulfanyl]phenyl}propionic Acid;

3-{2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-
ylmethylsulfanyl]phenyl}propionic Acid;

25 2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenoxyacetic
Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-
ylmethylsulfanyl]phenoxy}propionic Acid;

30

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-
ylmethylsulfanyl]phenoxy}propionic Acid;

35 2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-
ylmethoxy]phenoxy}propionic Acid;

- 180 -

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenoxy}propionic
5 Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

10 (+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

15 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

20

(2-Ethyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)acetic Acid;

25 (2-Methyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)acetic Acid;

2-Methyl-2-(4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

30

2-Methyl-2-(2-methyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

2-Methyl-2-(2-methyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

35

- 181 -

2-Methyl-2-(4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

5 2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenoxy}propionic Acid;

10 2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxy}propionic Acid;

15 2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenylsulfanyl}propionic Acid;

20 2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxymethyl]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethoxy}phenoxy)propionic Acid;

25 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethylsulfanyl}phenoxy)propionic Acid;

30 (+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethylsulfanyl}phenoxy)propionic Acid;

35 2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethoxy]phenoxy}propionic Acid;

- 182 -

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethoxy]phenylsulfanyl}propionic Acid;

5 2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethylsulfanyl]phenoxy}propionic Acid;

10 2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethoxy]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethoxy}phenoxy)propionic Acid;

15 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethoxy}phenylsulfanyl)propionic Acid;

20 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethylsulfanyl}phenoxy)propionic Acid;

25 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethoxy}phenoxy)propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenoxy}propionic Acid;

30 (+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

35 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

- 183 -

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

5 (+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethoxy}phenylsulfanyl)propionic Acid;

10 2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxy}propionic Acid;

15 2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxy}propionic Acid;

20 2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethoxy]phenoxy}propionic Acid;

25 (+/-)-2-Methyl-2-(2-methyl-4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

30 (+/-)-2-Methyl-2-(4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethoxy}phenylsulfanyl)propionic Acid;

35 (+/-)-2-Methyl-2-(4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

- 184 -

(+/-)-2-Methyl-2-(4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

5 (+/-)-2-Methyl-2-(2-methyl-4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butylsulfanyl}phenoxy)propionic Acid;

10 (+/-)-2-Methyl-2-(4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butoxy}phenoxy)propionic Acid;

15 (+/-)-2-Methyl-2-(2-methyl-4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methoxy}phenoxy)propionic Acid;

20 (+/-)-2-Methyl-2-(2-methyl-4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methoxy}phenylsulfanyl)propionic Acid;

25 (+/-)-2-Methyl-2-(4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methoxy}phenoxy)propionic Acid;

30 2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethoxy]phenoxy}propionic Acid;

35 2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethoxy]phenylsulfanyl}propionic Acid;

- 185 -

2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenoxy}propionic Acid; and,

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethoxy]phenoxy}propionic Acid.

50. A compound as claimed by any one of Claims 1 through 49 that is in the S conformation.

51. A compound as claimed by any one of Claims 1 through 49 that is in the R conformation.

52. A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by any one of Claims 1 through 51 together with a pharmaceutically acceptable carrier or diluent.

53. A method of modulating a peroxisome proliferator activated receptor, comprising the step of contacting the receptor with at least one compound as claimed by any one of Claims 1 through 51.

54. A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 51.

55. A method of treating Metabolic Syndrome in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 51.

- 186 -

56. A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by any one of Claims 1 through 51 to a mammal in need thereof.

5 57. The manufacture of a medicament for use in the treatment and/or prevention of a condition mediated by nuclear receptors, in particular by a peroxisome proliferator activated receptor, wherein the compound is a compound as claimed by any one of Claims 1 through 51.

10 58. A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by any one of Claims 1 through 51.

15 59. A method as claimed by Claim 58 wherein the mammal is diagnosed as being in need of such treatment.

20 60. A method of treating arthritis in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 51.

61. A method of treating demyelating disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 51.

25 62. A method of treating inflammatory disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 51.

30 63. A method as claimed by any one of Claims 60, 61, and 62 wherein such mammal is diagnosed as being in need of such treatment.

- 187 -

64. A compound as Claimed by any one of Claims 1 through 51 for use as a pharmaceutical.

5 65. A compound as claimed by any one of Claims 1 through 51 wherein the compound is radiolabeled.

66. A compound as disclosed by any one of the Examples herein.

10 67. All methods disclosed herein of preparing the compounds as claimed by any one of Claims 1 through 3.
